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Re-evaluation Note REV2017-08

2,4-D Update

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Update on 2,4-D

Introduction

2,4-dichlorophenoxy acetic acid, commonly known as 2,4-D is currently registered in Canada for use on turf, forests and woodlots, terrestrial feed and food crops, and industrial and domestic non-food sites.

In 2013, pursuant to subsection 17(2) of the *Pest Control Products Act*, the Pest Management Regulatory Agency (PMRA) initiated a special review of pest control products containing 2,4-D based on the decision taken by Norway in 2000 to prohibit the use of this active ingredient due to human health and environmental concerns. The aspects of concern that prompted the special review were related to human health (potential carcinogenicity of 2,4-D) and the environment (high mobility and the potential for runoff of 2,4-D to aquatic habitats from treated areas; potential risk to aquatic plants following runoff).

In 2016, following a science-based assessment of the above aspects of concern, the PMRA published the proposed special review decision for 2,4-D (REV2016-08). The proposed decision indicated that the pest control products containing 2,4-D were acceptable for continued registration taking into account the current conditions of use, and proposed to confirm the current registration.

Following the publication of REV2016-08, the Norwegian Food Safety Authority registered 2,4-D as a pest control product for use on turf in Norway as of April 2016.

Subsection 17(2) of the *Pest Control Products Act*

As 2,4-D is currently registered for use in Norway, the criteria for a special review pursuant to subsection 17(2) of the *Pest Control Products Act* are not met (that is, when an OECD member country prohibits all uses of a pesticide for health or environmental reasons), and consequently, no special review is required under subsection 17(2).

Subsection 17(1) of the *Pest Control Products Act*

The PMRA also received a request for special review under subsection 17(4) of the *Pest Control Products Act*. The request was based on the prohibition of 2,4-D in Norway in 2000 due to human health and environmental concerns as outlined above. Therefore, the information from the 2000 Norway decision was further assessed under subsection 17(1) of the *Pest Control Products Act*. There were no concerns related to the value of 2,4-D included in the 2000 Norway decision.

In order to evaluate the aspects of concern identified by Norway, the PMRA has considered the available information from Norway pertaining to the health and environmental concerns identified in the Norway decision. In addition, the PMRA considered the currently available relevant scientific information, which includes information considered for the re-evaluation of 2,4-D and any relevant information obtained since then, such as the information on Canadian incident reports, surface water monitoring data, reviews of epidemiological studies on 2,4-D and other phenoxy herbicides available in the public domain, available assessments of the potential

carcinogenicity of 2,4-D including the latest International Agency for Research on Cancer (IARC) hazard classification, assessments from the European Food Safety Authority and the United States Environmental Protection Agency (USEPA), and comments received during public consultation on the proposed special review decision for 2,4-D.

Regarding potential carcinogenicity of 2,4-D, as outlined in REV2016-08, the IARC classification of 2,4-D as a possible human carcinogen was based on "*strong evidence that 2,4-D induces oxidative stress that can operate in humans*" and moderate evidence that 2,4-D causes immunosuppression (IARC, 2016). IARC clearly indicated that "*the evidence that 2,4-D is genotoxic is weak*", and there was "*inadequate evidence in humans*" and "*limited evidence in experimental animals*" for the carcinogenicity of 2,4-D. Furthermore, the IARC classification is not a risk assessment. The levels of human exposure, which determine the actual risk, were not taken into account. Both the European Commission (2014) and USEPA (2014) considered 2,4-D as unlikely to be carcinogenic to humans. The available epidemiological studies continue to provide equivocal evidence for an association between exposure to 2,4-D (and other phenoxy herbicides) and cancer.

Taking into consideration available information, the fact that the weight of evidence from animal studies designed to show causality did not support a carcinogenic effect of 2,4-D, negative mutagenicity and genotoxicity studies, epidemiological studies providing equivocal evidence for an association between exposure to 2,4-D (and other phenoxy herbicides) and cancer, as well as the recognition that there are many other factors that may contribute to the etiology of the reported cancer cases, the PMRA has concluded that 2,4-D does not increase the risk of cancer under the current conditions of use. Based on the review of available information, the PMRA has concluded that there are no reasonable grounds to believe that 2,4-D may cause an unacceptable health risk under the current conditions of use in Canada.

In assessing high mobility and the potential for runoff of 2,4-D to aquatic habitats from treated areas, as well as the potential risk to aquatic plants following runoff, the PMRA considered the behaviour of different derivatives of 2,4-D (acid/amine group and the ester group) in the environment, as well as available information pertaining to the toxicity of 2,4-D forms to aquatic plants.

The PMRA determined that 2,4-D and the amine derivatives are very soluble in water and highly mobile, therefore, the potential for runoff from the treated areas into aquatic habitats would be high, following irrigation or rainfall. To minimize the potential runoff from treated areas into aquatic habitats, advisory label statements are currently included on the product labels advising the users of measures that can help reduce runoff.

The PMRA assessed potential risks to aquatic plants resulting from exposure to 2,4-D derivatives using the modeled estimated environmental concentrations (EECs), as well as the available robust surface water monitoring data for 2,4-D from Canada and the United States (including urban runoff data and the most recent (2002-present) surface water monitoring data). As part of aquatic risk assessment, risk quotients (RQ) for various derivatives of 2,4-D and use scenarios (turf, agricultural/non crop/forestry uses) are calculated based on the modeled EECs and relevant aquatic endpoints and, then, are compared to the PMRA's Level of Concern (LOC) of 1.

Conservative assumptions are used to derive modeled EECs (for example, maximum number of applications and minimum intervals between applications).

For turf uses and agricultural uses, the calculated RQs (0.04 to 2.0) exceeded the PMRA's LOC based on modelled EECs. In addition to the modeled EECs, the PMRA considered available surface water monitoring information, which indicated that the risk to aquatic plants is, in fact, deemed to be unlikely. Based on the highest concentration detected in Canada in urban runoff (0.0469 mg/L), and in the most recent surface water monitoring (0.011 mg/L), and the most appropriate endpoints for aquatic plants for different derivatives of 2,4-D , the actual risk to aquatic plants is below the PMRA's LOC and, therefore, not of concern. Based on the above, the PMRA has concluded that there are no reasonable grounds to believe that 2, 4-D may cause an unacceptable environmental risk under the current conditions of use in Canada.

Consequently, the PMRA has concluded that there are no reasonable grounds to believe that the human health and environmental risks of products containing all forms of 2,4-D currently registered in Canada are, or their value is, unacceptable under current conditions of use. On this basis, a special review is not required under subsection 17(1) of the *Pest Control Products Act*.

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